GENETIC POLYMORPHISM OF DRUG METABOLIZING ENZYMES AND ESTROGEN RECEPTOR IN PHARMACOGENETICS OF TAMOXIFEN: IMPLICATION FOR OPTIMIZATION OF BREAST CANCER TREATMENT

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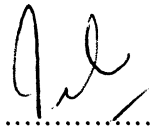

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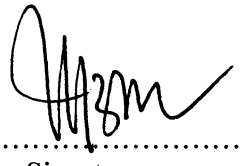

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Abstract

Introduction: Tamoxifen has been used as a hormonal therapy in breast cancer patients who are positive for estrogen receptor. The drug is metabolized by Cytochrome P450 2D6 (*CYP2D6*) into several metabolite. Variation in *CYP2D6* activity has important therapeutic consequences and can play a significant role in the development of adverse events or therapeutic failure in susceptible individuals. Beside, variation of drug transporter such as *MDR1* may alter the accumulation of the drug and cause toxicity in patients. Furthermore, the different expression of receptor-α and estrogen receptor-β may be associated with different therapy outcome.

Materials and methods: In subject recruitment, patient samples were collected from HUKM, Hospital Selayang and HTAF. Patients who have received tamoxifen for treatment of breast cancer were recruited according to exclusion and inclusion criteria. Genotyping method for *CYP2D6* and *MDR1* were developed using multiplex allele specific PCR (ASPCR) approach. DHPLC method was developed to detect existing and new alleles in *CYP2D6* and estrogen receptors. The expression of estrogen receptor-α and estrogen receptor-β from samples would be quantitated using Real-time PCR.

Result: The most common variants detected is *CYP2D6*10* with 50% of heterozygous *CYP2D6*1/*10* and *CYP2D6*5* with 7.8% was detected high in breast cancer patients. Furthermore *CYP2D6*1/*4* and *CYP2D6*1/*4* was detected but at low frequencies.

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